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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/777,856	02/07/2001	Ami Aronheim	01/21605	3362

7590 01/26/2006

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EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 01/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/777,856	ARONHEIM ET AL.	
	Examiner	Art Unit	
	Maria B. Marvich, PhD	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/21/05*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6-11,15-20,24-29 and 33-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6-11,15-20,24-29 and 33-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 June 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to an amendment filed 11/21/05. Claims 3-5, 12-14, 21-23, 30-32 and 36-49 have been cancelled. Claims 1, 6, 9, 15, 18, 24, 27 and 33 have been amended. Claims 1-2, 6-11, 15-20, 24-29 and 33-35 are pending.

Response to Amendment

Any rejection of record in the previous action not addressed in this office action is withdrawn. The new grounds of rejection herein were necessitated by amendment and, therefore, this action is final.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9, 15-20, 24-29 and 33-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The limitation that the cell lacks "**a** Ras signaling" has been added to claims 9, 18 and 27. **This is a new rejection necessitated by applicants' amendment.**

Applicant has not indicated where support for the limitation "**a** Ras signaling" is found. The examiner has been unable to find literal support in the originally filed specification for the term "a Ras signaling". On page 21, the specification teaches that a cytoplasmic Ras mutant refers to a Ras mutant protein lacking a membrane-targeting signal and thus is incapable of targeting to the plasma membrane. Hence Ras signaling is abolished. The limitation that the cell lacks **a** Ras signaling is distinct as the cell can possess some Ras signaling and not others. Ras signal transduction pathways are complex, multi-subunit, interacting pathways. Disruption of any part of the Ras signaling pathway other than Ras mutants is not taught. The specification does not teach that a component of the signaling can be abolished. Therefore, the limitation of "a Ras signaling" is impermissible NEW MATTER.

Response to Argument

Applicants traverse the claim rejections under 35 U.S.C. 112, first paragraph on pages 11 of the amendment filed 11/21/05. Applicants argue that the claim has been amended to recite use of cell(s) lacking "Ras signaling".

Applicants' arguments filed 11/21/05 have been fully considered but they are not persuasive. Claims 9, 18 and 27 have been amended to recite that the cell or cells lack "**a** Ras signaling". The specification does not provide a description or guidance for cells or a cell that lack a Ras signaling. In this case, a single signaling pathway of Ras would need to be identified and characterized and cells in which the specific Ras signaling is missing generated. In fact, the specification only teaches that cells lack Ras activity (suggested to be Ras signaling), which is restored upon interaction of a Ras mutant with the cytoplasm.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-2, 6-11, 15-20, 24-29 and 33-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **These are new rejections necessitated by applicants' amendment.**

Claims 1, 9, 18 and 27 recites the limitation "said Ras activity" in 1. There is insufficient antecedent basis for this limitation in the claim. **This is a new rejections necessitated by applicants' amendment.**

Claim 9 is vague and indefinite in that the metes and bounds of "indicative of an interaction between said first polypeptide and said distinct polypeptide" are unclear. The method involves expressing a library of polynucleotides each of which encodes a distinct polypeptide in cells. As multiple library members can be in each cell, it is unclear how **an** interaction between the first polypeptide and distinct polypeptide can be distinguished given that other interactions between distinct polypeptides and the first polypeptide are possible within the same cell. **This rejection is maintained for reasons of record in the office action mailed 4/19/05.**

Claims 9, 18 and 27 are vague and indefinite in that the metes and bounds of "identifying said Ras signaling" are unclear. The cell lacks only a Ras signaling and hence it would not be expected that all of Ras signaling is abolished in the cell. Therefore, as Ras signaling as a whole

is not abolished, it is unclear how Ras signaling would only be functional under inductive conditions but not under non-inductive conditions. **This is a new rejection necessitated by applicants' amendment.**

Response to Argument

Applicants traverse the claim rejections under 35 U.S.C. 112, second paragraph on pages 10-11 of the amendment filed 11/21/05. Applicants' argue that only one interaction between a bait polypeptide and a prey polypeptide is possible as each member of the library is expressed in a specific cell of a plurality of cells.

Applicants' arguments filed 11/21/05 have been fully considered but they are not persuasive. The claims recite that a library of polynucleotides is expressed in cells each encoding a "distinct" polypeptide. However, any cell could express several "distinct" polypeptides. And so it is not clear how one such interaction could be distinguished from another. First, it is unclear what is intended by "distinct" as this is a relative term. Secondly, if applicants intend that each cell expresses one polypeptide from the library, it would be remedial to recite that.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 6-8, 27-29 and 33-35 are rejected under 35 U.S.C. 102(a) as being anticipated by Takemaru and Moon, The Journal of Cell Biology 149(2), April 17, 2000, pages 249-254, see entire document. **This rejection is maintained from the office action mailed 2/5/04 and 8/24/04 and 4/19/05 and has been reworded based upon applicants' amendment.**

Takemaru and Moon teach a method of identifying interactions between polypeptides comprising use of cdc25-2 yeast strain (endogenous ras is inactive and therefore the cell will lack Ras signaling and a Ras signaling). The cells were transfected with a first polynucleotide under control of an inducible promoter encoding a polypeptide capable of interacting with a plasmalemma. This construct is library cDNA fused to v-Src myristoylation sequences and under control of the galactose inducible promoter (page 250, col2, paragraph 2 and page 251, col 1, paragraph 3). The cells were transfected with a second polynucleotide comprising a fusion of a second polynucleotide and a Ras cytoplasmic mutant. This vector is pRas(61)ΔF-βcatR8-C an expression vector comprising c-HaRas mutant fused to β-catenin in a (see e.g. page 251, column 1, paragraph 3). Cells were grown under inductive conditions, minimal galactose, and non-inductive conditions, minimal glucose. It is the difference between the two that indicates an interaction between a first and second polypeptide. Following growth of cells under inductive and non-inductive conditions, a clone expressing CBP in complex with b-catenin was identified upon isolation of a subset of cells (see e.g. page 251, column 1, paragraph 4) as in claim 28. The cdc25-2 cells are growth suppressive under non-permissive temperatures as in instant claim 6

and 33. This phenotype is corrected by translocation of the Ras mutant to the plasmalemma as in instant claim 7 and 34.

The v-Src myristoylation sequence is native to a v-Src gene and therefore meets the limitations of claim 2 and 28. Therefore, the library cDNAs fused to the v-Src myristoylation is on a vector that comprises an inducible galactose promoter driving expression of a first polypeptide. The art has been applied as if this vector meets the limitation of claim 1 in that this is one polypeptide, which is a fusion between two polypeptide sequences and has been applied to meet the limitation of claim 27 in that v-Src is one polypeptide and the library cDNA encodes the second polypeptide.

Response to Arguments

Applicants traverse the claim rejections under 35 USC 102(a) on pages 10-12 of the amendment filed 11/21/05. Applicants argue that the instant invention utilizes a step that distinguishes from interaction-independent translocation of Ras to the cell membrane. Applicants continue that the Examiner has mistaken replica plating as the equivalent of selective library protein expression utilized in the present invention. While, the intent invention utilizes replica plating, it is profoundly different than that practices by Takemaru and Moon. Applicants point to the identification of the method as RRS and the teachings on page 251, col 1 as evidence of the distinction between the two. In this passage, Takemaru and Moon teach that the plasmid encoding CBP was recovered and retransformed into the same yeast strain with either an expression plasmid for Ras(61) or a negative control plasmid as confirmation.

Applicants' arguments filed 2/24/04 have been fully considered but they are not persuasive. While applicants state that a step is present in the instant invention that is not present in that of Takemaru and Moon and this step is "selective library plating", it is not clear what is actually entailed in this step. It appears as if this step is the use of an inducible on/off promoter. However, Takemaru and Moon use an inducible promoter, which is off under conditions of minimal glucose then turned on in the presence of galactose. Page 250, col 2, paragraph 2 teaches "Positive clones exhibiting efficient growth on galactose plates at 37°C were isolated and tested for galactose dependent growth at 37°C". Hence, the actual distinction between the two inventions is not apparent from the recited claims. As recited the instant invention is anticipated by Takemaru and Moon. That confirmation of the results is undertaken or that the method is called RRS does not effect this as the instant claims using "comprising" which is open language do not occlude RRS or confirmation through other steps.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B. Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, David Nguyen, PhD can be reached on (571)-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1633

January 21, 2006

DAVE TRONG NGUYEN
SUPERVISORY PATENT EXAMINER